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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 18

Application Number: 09/467,100
Filing Date: December 10, 1999
Appellant(s): COLEMAN ET AL.

Susan K. Sather
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed on 6/15/02.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

The summary of invention contained in the brief is substantially correct however, it includes comments (i.e., appellants' statement regarding the function of the polynucleotide of SEQ ID NO:1 as having a variety of utilities , in particular expression profiling, diagnosis of conditions or diseases, toxicology testing, drug discovery and chromosome mapping) on the merits of the rejection as well as simply a summary of the claimed invention. Such statements are appropriately found in the arguments section of the brief and will be addressed in the Response to Arguments section of this Answer.

(6) Issues

The appellant's statement of the issues in the brief is correct with regards to Issue 1 (scope of enablement rejection under 35 USC 112, first paragraph), Issue 2

(written description rejection under 35 USC 112, first paragraph), Issue 3 (written description rejection under 35 USC 112, first paragraph with respect to new matter), Issue 4 (obviousness rejection under 35 USC 103), Issue 5 (double patenting rejection under 35 USC 101), and Issue 6 (double patenting rejection under 35 USC 101).

(7) Grouping of Claims

The appellant's statement in the brief that claims stand or fall together for each of the issues on appeal is correct.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

Silvennoinen et al. Proc. Natl. Acad. Sci. USA (1993) 90, 8429-8433.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Issue One: Scope of enablement rejection under 35 USC 112, First paragraph

Claim 36-40 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide comprising a polynucleotide sequence of SEQ ID NO: 1, or a polynucleotide sequence having at least 92% sequence identity to the polynucleotide sequence of SEQ ID NO: 1, wherein said polynucleotide encodes a polypeptide which has kinase activity, does not

reasonably provide enablement for any isolated polynucleotide comprising a polynucleotide sequence having greater than 92 % sequence identity to SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claim 36 (37-40 dependent from) is so broad as to encompass any polynucleotide comprising a polynucleotide sequence which is a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO: 1 (Claim 36 b)or its complementary polynucleotide sequence (Claim 36 d), while claims 37-40 recite methods of use of such polynucleotides and fragments thereof. The scope of the claim is not commensurate with the enablement provided by the disclosure with regard to the utility of the polynucleotides broadly encompassed by the claims including many polynucleotides which are not expressed nor encode proteins. It would require undue experimentation of the skilled artisan to use the majority of the claimed polynucleotides comprising a

polynucleotide sequence which is a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO: 1 or its complementary polynucleotide sequence. The specification is limited to teaching the use of "said polynucleotides" which encode a human Jak2 kinase polypeptide as an enzymatic catalyst and provides no guidance with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make the claimed polynucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. A naturally occurring amino acid sequence having at least 92% sequence identity to the polynucleotide sequence of SEQ ID NO: 1 " encompasses polynucleotide variants encoding naturally occurring orthologs in related species, particularly human polypeptide variants with mutations that result in altered activity. It is unclear what function a polypeptide variant with a mutation that results in "altered activity" has and absent a teaching of this "specific altered activity", how the polynucleotides which encode these polypeptides are enabled with respect to there use. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polynucleotides encompassed by this claim.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polynucleotide comprising a polynucleotide sequence which is a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO: 1

(Claim 36 b)or its complementary polynucleotide sequence. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The inclusion of language such as wherein the polypeptide has kinase activity may help applicants overcome problems presented above with respect to the utility of claimed DNA.

Issue Two: Written Description rejection under 35 USC 112, First paragraph

Claim 36-40 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 36 is directed to all possible polynucleotides comprising a polynucleotide sequence which is a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO: 1 (Claim 36 b)or its complementary polynucleotide sequence (Claim 36 d) which encompasses allelic variants of SEQ ID NO: 1, while claims 37-40 recite methods of use of these polynucleotides or fragments thereof.

There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these polynucleotides by any identifying functional characteristics or properties. Since the claimed genus encompasses polynucleotides yet to be discovered, polynucleotide constructs that encode fusion proteins, etc., the disclosed structural feature of SEQ ID NO: 1 does not "constitute a substantial portion" of the claimed genus. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Further, Claim 36 encompasses "allelic sequences". An "allelic sequence" is an alternative form of the gene which may result in at least one mutation in the nucleic acid sequence. Alleles may result in altered mRNA or polypeptides whose structure or function may or may not be altered. This definition does not provide any specific information about the structure of naturally occurring (alleles) variants of SEQ ID NO: 1 (i.e. where are the regions within which mutations are likely to occur) nor discloses any function for naturally occurring variants. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO: 1 relates to the structure of any naturally occurring alleles. The general knowledge in the art concerning alleles dose not provide any indication of how one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art structure of one does not provide guidance to the structure of

others. The genus of polynucleotides that comprise the claimed polynucleotide molecules is a large variable genus with potentiality of encoding many different proteins. Therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus (i.e. the sequence of SEQ ID NO: 1) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Issue Three: Written Description rejection under 35 USC 112, First paragraph

Claims 36-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitation in claim 36 (37-40 dependent from) of "greater than 92% identity" is rejected as being new matter that is not supported by the original specification. Applicants submission that the specification at page 3, lines 31-34 and page 7, lines 20-26 indicates that applicants envisioned Jak2 kinase variants of greater than 92% sequence identity to murine Jak2 kinase is not persuasive. It is acknowledged that at

page 7, applicants envision a "recombinant polypeptide variant" and at page 3, applicants recognize that "HJAK2 has 92% similarity to murine Jak2" but applicants suggestion that "applicants envisioned Jak2 kinase variants of greater than 92%" is not persuasive.

Issue Four: Obviousness rejection under 35 USC 103(a)

Claims 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Silvennoinen et al.

Silvennoinen et al. teach the structure of the murine Jak2 protein-tyrosine kinase and its role in interleukin 3 signal transduction. They specifically teach the cloning of a full-length cDNA clone for murine Jak1 and Jak2 protein-tyrosine kinase. A comparison of the amino acid sequence of the murine Jak2 protein shows that its best local similarity is 93.3% with that of SEQ ID NO: 2. These cDNAs were inserted into pBSK plasmid to make transcripts with T3 RNA polymerase (See page 8430, top of column 1). Further, the polynucleotide taught by Silvennoinen et al. encodes a polypeptide comprising a naturally occurring amino acid sequence, as well a biologically active and immunogenic fragments of an amino acid sequence of SEQ ID NO: 2.

One of ordinary skill in the art at the time of filing would have been motivated to use the sequence taught by Silvennoinen et al. to design oligomers for use as primers to amplify and determine the level of mRNA encoding the murine Jak2 protein or to isolate other mRNAs encoding related proteins such as human Jak2 using hybridization or polymerase chain reaction methodology. As discussed above and in the previous

office action, and seen in the comparison of the sequence of SEQ ID NO: 1 with the murine Jak2 cDNA, there exists many regions of 100% identity between the two cDNAs. It is noted that it is a common practice in the art to design oligomers such that they do not correspond exactly to the sequence on which they are based. For instance often they are degenerate in order to identify additional members of a family and they incorporate additional bases for cloning, etc. Thus an oligomer of the polynucleotide comprising the nucleic acid sequence of SEQ ID NO: 1 is made obvious by Silvennoinen et al. Further, one of ordinary skill in the art would have been motivated to use these oligomers as part of a method for detecting the level of murine and human Jak2 mRNAs in tissue samples or identifying additional related mRNAs. Further motivation for the design and use of oligomers based on murine Jak2 is that Silvennoinen et al. teach that the Jak2 protein is regulated in response to IL-3 and is involved in signal transduction associated with hematopoiesis and there interest in the role of Jak1 and Jak2 genes in IL-3 signal transduction.

Issue Five: Double Patenting rejection under 35 USC 101

Claims 30-36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-3 of U.S. Patent No. 5,914,393. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent and the application are claiming common subject matter, as follows: A purified polynucleotide consisting of a nucleic acid sequence encoding the polypeptide of SEQ ID NO: 2.

Issue Six: Double Patenting rejection under 35 USC 101

Claims 37-40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of U.S. Patent No. 5,914,393. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of detecting a polynucleotide comprising a sequence of SEQ ID NO: 1 or variants thereof (claims 37-40) is obvious over claims to the polynucleotide consisting of SEQ ID NO: 1 or the complement thereof (claims 1-3). Claims 37-40, drawn to methods of detecting a polynucleotide comprising a sequence of SEQ ID NO: 1 or variants thereof are obvious over claims to the polynucleotide

consisting of SEQ ID NO: 1 or the complement thereof (claims 1-3), because one of ordinary skill in the art would be motivated to design PCR and hybridization probes based on the sequence of SEQ ID NO: 1 for use in methods of detecting the presence and level of polynucleotides encompassed by and related to SEQ ID NO: 1. The motivation for such methods is they would be useful for the characterization of these nucleic acid sequences and the role they play in natural physiology and/or disease such that this information could be used to treat or enhance these conditions.

(11) Response to Argument

Issue One: Scope of enablement rejection under 35 USC 112, First paragraph

Appellants submit that the rejection of claims 36-40 under 35 USC 112, First paragraph is improper because the specification provides an enabling disclosure for the claimed subject matter. The enablement requirement of 35 U.S.C. 112 first paragraph, provides that an applicant must describe how to make and use what is claimed. Appellants correctly point out that one of skill could make the subject matter encompassed by the claims and that the claims remain rejected because the specification does not describe how to use the subject matter defined by the claims. The appellants submit that the invention at issue is a polynucleotide sequence corresponding to a gene that is expressed in human placenta tissue as well as its naturally-occurring polynucleotide variants. The appellants submit that the novel SEQ ID NO: 1 polynucleotide [en]codes for a polypeptide demonstrated in the specification to

be a member of the class of Jak kinases, whose biological function include phosphorylating proteins on tyrosine residues. As previously stated "a naturally occurring amino acid sequence having at least 92% sequence identity to the polynucleotide sequence of SEQ ID NO: 1 " encompasses polynucleotide variants encoding naturally occurring orthologs in related species, particularly human polypeptide variants with mutations that result in altered activity. It is unclear what function a polypeptide variant with a mutation that results in "altered activity" has and absent a teaching of this "specific altered activity", how the polynucleotides which encode these polypeptides are enabled with respect to there use. Appellants assert as such the claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease, none of which requires knowledge of how the polypeptides [en]coded for by the polynucleotides actually function. Appellants submit as a separate paper with this brief, the Declaration of Dr. Tod Bedilion, which for the purpose of this answer have not been considered. Appellants further assert that the law never has required knowledge of biological function to prove utility, and that it is the claimed invention's uses, not its functions, that are the subject of a proper analysis under the enablement requirement. Appellants submit that the uses of the claimed polynucleotides are for diagnosis of conditions and disorders characterized by expression of HJAK2, for toxicology testing and for drug discovery and that these are sufficient utilities under 112 first paragraph. Appellants submit a number of references that discuss the benefits of these various methodologies such as "differential gene expression","toxicogenomics" and "expression profiling", but Appellants give no

guidance as to how those claimed polynucleotides which do not encode a polypeptide having Jak2 kinase activity are so useful. Appellants disclose no specific examples of such uses, but rather assert that the claimed polynucleotides, a majority of which have no "functional" limitation, may be useful for such general techniques as "expression profiling" and "drug development". Appellants give none of the particulars of toxicology testing with the claimed polynucleotides having greater than 92% identity to SEQ ID NO: 1. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or polynucleotides, but is only potential with respect to the claimed polynucleotides. Further any potential diagnostic utility is not yet known and has not yet been disclosed.

Appellants' arguments have been fully considered but are not found persuasive to overcome the rejection.

The rejection is not based on a difficulty of determining how to make those polynucleotides having greater than 92% identity to SEQ ID NO:1, but on the difficulty of determining a use of all polynucleotides encompassed by the claimed genus. The functional activity of a polypeptide is dependent on its structure, therefore, a polynucleotide comprising an nucleotide sequence having greater than 92 % identity to SEQ ID NO:1 will not necessarily encode a polypeptide retaining Jak2 kinase activity.

In regards to using the polynucleotides of claim 36 parts b) and d), appellants argue the specification provides a number of uses for the claimed polynucleotides of claim 36 parts b) and d) and specifically asserts toxicology testing, drug development,

and the diagnosis of disease as examples of such uses. Appellants argue these uses are well-established in the art and as a result of their benefits, enjoy commercial success. Appellants argue the examiner has failed to address these uses in the final Office action of Paper No. 12. Appellants' argument has been fully considered but is not found persuasive to overcome the rejection.

The specification does not disclose any of the claimed *variant* polynucleotides (nor even SEQ ID NO:1) as markers for a specific disease state. Absent a disclosure of altered levels, structure, or function of a polynucleotide in a diseased cell or tissue as compared with the corresponding healthy cell or tissue, the polynucleotides of claim 36 parts b) and d) are not indicative of a disease state and do not provide an appropriate target for drug discovery or toxicology testing. Guidance relating the claimed polypeptide variants to a specific disease state is necessary for the asserted uses of toxicology testing, drug development, and the diagnosis of disease. As this guidance has not been provided, it would necessarily require undue experimentation for a skilled artisan to test each of the infinite number of polynucleotides of claim 36 parts b) and d) for altered levels, structure, or function in a diseased cell or tissue as compared with the corresponding healthy cell or tissue. Thus, even if one conceded that SEQ ID NO:1 could be used for these purposes without undue experimentation (which is not conceded herein but irrelevant in the instant case as the specification does teach a use of SEQ ID NO:1, i.e., (encoding a polypeptide with kinase activity) one could not use the full scope of claimed variants for these purposes without undue experimentation. Finally, evidence of commercial success, while potentially persuasive as secondary

evidence of non-obviousness, is immaterial to the instant scope of enablement rejection.

Appellants argue that in recent years, techniques have been developed for toxicology testing, drug development, and disease diagnosis. Appellants argue these techniques rely on gene expression profiling by analyzing the relative levels of genes or proteins present in two or more samples. Appellants provide a number of citations in support of their argument of the prevalence, advantages, and importance of gene expression profiling in toxicology testing, drug development, and disease diagnosis, however for the purpose of this brief, these references have not been considered because these appellants have not shown good and sufficient reasons why they were not presented earlier (See Paper No. 17). Appellants' argument has been considered but is not found persuasive to overcome the rejection.

While it is well-established that techniques such as toxicology testing, drug development, and disease diagnosis may be useful, as previously stated, the instant specification has not established the claimed polynucleotide variants (or even SEQ ID NO:1) as having altered expression levels or expressed in altered forms in a diseased cell or tissue relative to the corresponding healthy cell or tissue. The instant specification has not established increased expression levels or forms of any of the polynucleotides of claim 36 parts b) and d) and therefore, undue experimentation would be required to use the claimed polynucleotide variants for the asserted uses. Therefore, the polynucleotide variants as encompassed by the claims will not necessarily be useful in the same fashion as SEQ ID NO:1 nor in toxicology testing, drug development, and

disease diagnosis as argued by appellants and, in fact, the vast majority of such variants may not be useful at all. As such, the scope of the claims remains broader than the scope of the enabling disclosure.

Therefore, for above reasons, it is believed that the rejection should be sustained.

Issue Two: Written Description rejection under 35 USC 112, First paragraph

Appellants argue that the written description standard is fulfilled by what is specifically disclosed and what is conventional or well known to one skilled in the art. Applicants assert that the present claims specifically define the claimed genus through the recitation of chemical structure. As noted in the above rejection and earlier responses, the recited chemical structure in and of itself is sufficient, but what is lacking is a functional description of the claimed genus such that applicant have adequately described the claimed genus. Appellants argue there is no requirement that claims recite particular variant and fragment sequences as claimed because the claims provide a sufficient structural definition of the claimed polynucleotides. Appellants argue that based on the structural definition of the variants and fragments provided in the claims, one of skill in the art can discern the structure of all claimed polypeptides. Appellants argue that listing all claimed variants and fragments in the specification would "needlessly clutter" the specification. Appellants argue the examiner's position is "nothing more than a misguided attempt to require Appellants to unduly limit the scope of their claimed invention". Appellants' arguments have been fully considered but are not found persuasive to overcome the instant rejection.

The examiner fully acknowledges appellants' recitation of the structural limitations of the polypeptides of claim 36 parts b) and d) and appellants' attempts to claim polynucleotides based solely on the structural definitions as recited in claim 36 parts b) and d). However, the polynucleotides as defined in claim 36 parts b) and d) encompass a genus of polynucleotides that encompasses widely variant species, some having the same functions as the polynucleotide of SEQ ID NO:1, some having unknown and distinctly different functions and some possibly having no function. While one of skill in the art, provided the sequence of SEQ ID NO:1, may be able to recognize variants of SEQ ID NO:1 with an nucleotide sequence sharing greater than 92 % identity, one cannot recognize which of these variants occurs naturally and is thus encompassed by the genus of claim 36 part b). Therefore, the skilled artisan would not be able to envision all of the member of the claimed genus of polynucleotides merely from its structural limitations. This enormous genus will encompass a wide variety of polynucleotides with their own distinct properties. Because appellants have provided no functional limitation for the claimed polynucleotides, the single disclosed polynucleotide of SEQ ID NO:1 is not representative of the entire genus and one of skill in the art would *not* recognize that appellants were in possession of all polynucleotides comprising a naturally-occurring polynucleotide having greater 92 % identity to SEQ ID NO:1.

Appellants argue (part B at page 23 of the Appeal Brief) the polynucleotides of claim 36 parts b) and d) do not define a genus that is "large" and "variable" as appellants assert that available evidence illustrates the claimed genus of polypeptides as being of narrow scope. In support of appellants' assertion, appellants rely on the

teachings of Brenner et al. (Proc Natl Acad Sci USA 95:6073-6078, 1998,) which for the purpose of this brief has not been considered (See above statements regarding non-entry of references after final and Paper No. 17). Appellants' arguments have been fully considered but are not found persuasive to overcome the instant rejection.

As written, claim 36 part b) encompass *all* alleles - both functional and non-functional of SEQ ID NO: 1. The prediction of the function of the polypeptide encoded by SEQ ID NO:1 was *not* questioned. However, the disclosure of a single allele of a gene by structure and function does not provide a description of *all* alleles of the same gene as these alleles vary substantially in functional properties. Consequently, one of skill in the art would not expect the structural and functional description of a single polynucleotide sequence to be representative of *all* polynucleotides comprising a naturally-occurring nucleotide sequence with greater than 92 % nucleotide sequence to SEQ ID NO:1. Thus, the polynucleotides of claim 36 parts b) and d) constitute a large and variable genus.

Appellants argue (part A at pages 21-22 of the Appeal Brief) the instant claims are fundamentally different from the types of claims the court has found to lack sufficient written description as the instant claims recite a genus of polypeptides in strictly structural terms while the claims found to lack written description in cases such as *Fiers v. Revel* (25 USPQ2d 1601) and *University of California v. Eli Lilly and Co.* (43 USPQ2d 1398) defined the claimed genus in strictly functional terms. Appellants argue the instant claims define the polynucleotides of claim 36 by chemical structure and not function as in the claims found to be invalid in the *Lilly* and *Fiers* cases. Appellants argue the Office

action has failed to base its written description inquiry on "whatever is now claimed" and did not provide an analysis of how the instant claims differ from those of *Lilly* and *Fiers*. Appellants further argue the state of the art at the time of the invention is further advanced than at the time of the *Lilly* and *Fiers* cases. Appellants argue the techniques and technological advances since the *Lilly* and *Fiers* up to the filing of the instant application in combination with the teachings provided in the instant specification are such that one of skill in the art would recognize that appellants were in possession of the claimed polynucleotides. Appellants' argument has been fully considered but is not found persuasive to overcome the rejection.

While it is acknowledged that the current claims differ from those held by the court to lack sufficient written description, as discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show appellants were in possession of the claimed genus. A representative number of species means that the species that are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in

the art would recognize that appellants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus that embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case, the claimed genus of polynucleotides of claim 36 part b) and d) includes species which are widely variant in function. A polynucleotide comprising a naturally-occurring nucleotide sequence having greater than 92% identity to SEQ ID NO:1 includes allelic variants of SEQ ID NO:1 and all other loci having greater than 92% identity to SEQ ID NO:1. Allelic variants encompass polynucleotides *whose function may or may not be altered.* As such, neither the description of the structure and function of SEQ ID NO:1 nor the disclosure of solely structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus of claimed polynucleotides. While advances in the art are undeniable and widely recognized, the point of the rejection is lack of written description and not lack of enabling disclosure. The state of the art still does not allow one of skill in the art to predict the structure and function of existing naturally-occurring variants or polynucleotides comprising polynucleotide sequence greater than 92% identity to SEQ ID NO:1, based solely on a single disclosed polynucleotide structure. Most importantly, one skilled in the art would not be able to divine the functions of other naturally-occurring sequences of the claimed genus based on the knowledge of the function of only one disclosed species. It is noted that the claims of the '740 patent of the *Lilly* case were limited by *both* structural and

functional limitations (see for example claim 4 of '740), thus placing the artisan in possession of the attributes and features of all members of the claimed genus.

Therefore, for above reasons, it is believed that the rejection should be sustained.

Issue Three: Written Description rejection under 35 USC 112, First paragraph with respect to new matter

Appellants argue that consideration of the originally filed application shows that Appellants were in possession of what is now claimed, i.e. "a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO: 1". Appellants point to a specific passage of the specification to assert this position. Appellants submit that while the originally filed application does not contain a verbatim recitation of the present "92% sequence identity" claim language, it is apparent that the inventors contemplated naturally occurring polynucleotide and polypeptide sequences of Jak2 kinase molecules and that the inventors were aware that the Wilks Jak2 kinase had 92% similarity to the amino acid sequence of SEQ ID NO: 2. Appellants argue that it is therefore axiomatic that the present inventors considered naturally occurring polynucleotide sequences having "greater than 92% sequence identity" to the polynucleotide sequence of SEQ ID NO: 1, as part of their own invention. Appellants argument has been considered and is not

found persuasive. The mere mention of "the prior art having 92% identity" to the disclosed polynucleotide does not in any way support a position that appellants envisioned their invention to encompass all polynucleotides with greater homology to SEQ ID NO: 1 then the most similar sequence in the prior art and thus a claim to a polynucleotide sequence of "greater than 92% identity". While appellants clearly envisioned "variants" of SEQ ID NO: 1, the specification does not provide support for subgenera thereof based on % sequence identity and nowhere provides any reference to the currently claimed specific subgenus.

Therefore, for above reasons, it is believed that the rejection should be sustained.

Issue Four: Obviousness rejection under 35 USC 103(a)

Appellants submit that the examiner has mischaracterized Appellants' claims and continues to fail to give proper consideration to the entire claim in making the rejection. Appellants note that each of claims 37-40 are drawn to methods of detecting specific polynucleotides, as the preamble to the claim contains the limitation "said target polynucleotide having a sequence of a polynucleotide of claim 36".

Appellant further submits that the rejection fails to state a proper *prima facie* case of obviousness, and that the rejection should, therefore, be reversed.

Appellant is reminded that they refer to the claimed method as one for detection of the polynucleotides of claim 36 (those polynucleotides having greater than 92%

identity to SEQ ID NO: 1), exclusively. However, the steps recited in the claimed method do not result in exclusive detection of the polynucleotides of claim 36. This is because a probe comprising at least 16 contiguous nucleotides of a sequence complementary to said target polynucleotide (the polynucleotide s of claim 36), is not specific enough to detect only the polynucleotides of claim 36. The only means of rendering the claim exclusive for the detection of the polynucleotides of claim 36 is to utilize a probe comprising the polynucleotides of claim 36.

Therefore, due to aforementioned reasons, the invention as currently recited is directed to a method of detecting a large quantity of target polynucleotides using a fragment of SEQ ID NO:1, as probe in a hybridization assay, wherein said target polynucleotides comprise the polynucleotides of claim 36 and does not exclude other target polynucleotides which may also be detected by hybridization to the recited probe. The recitation of the preamble cannot be said to "breathe life" into the remainder of the claim as the remaining steps themselves can never achieve the detection of only the polynucleotides of claim 36. These steps can only achieve the detection of polynucleotides which comprise sequences 100 % sequence identity to whatever is used as a probe. In this case a fragment of the polynucleotide of claim 36. Thus the steps can only achieve detection of all those polynucleotides which comprise a fragment of the polynucleotide of claim 36. No matter how stringent one makes the hybridization, all such polynucleotides will hybridize.

Finally, with respect to appellant 's argument that a prima facie case of obviousness has not has been established, the examiner would like to indicate that in

contrast to appellants position, the following three criteria (i.e. motivation, reasonable expectation of success and the prior art teaching or suggestion of all claim limitations) are met for the following reasons:

The fact that the cDNA sequence of Silvennoinen et al. explicitly teach the gene encoding murine Jak2 protein-tyrosine kinase and its role in interleukin 3 signal transduction definitely motivates one of ordinary skill in he art to use said sequence as a probe in a hybridization assay to measure the level of murine Jak2 gene expression associated with signal transduction and identify additional related Jak2-type kinase genes in murine and other species (i.e. homo sapiens). Thus, clearly the motivation is present. Considering the level of knowledge in the prior art, it is merely routine experimentation to use a probe in a hybridization assay in order to detect target polynucleotides in unknown samples. Hence, there definitely is a reasonable expectation of success in using said probe in an assay to detect target polynucleotides. Finally, considering the high degree of similarity between the gene taught by Silvennoinen et al. and that of instantly disclosed, SEQ ID NO: 1, and the many contiguous regions of 100% identity with the disclosed SEQ ID NO: 1, there is no question that the obvious hybridization methods would have detected applicants claimed polynucleotides.

Therefore, for above reasons, it is believed that the rejection should be sustained.

Issue Five: Double Patenting rejection under 35 USC 101

Appellants have indicated the willingness to submit a terminal disclaimer with respect to U.S. Patent No. 5, 914,393, to overcome this rejection and have requested an indication that such a filing is sufficient to overcome the rejection. As was previously stated, such a filing of a terminal disclaimer would be sufficient to overcome this rejection, however, no TD has been filed at the present time, thus the rejection is maintained.

Issue Six: Double Patenting rejection under 35 USC 101

Appellants have indicated the willingness to submit a terminal disclaimer with respect to U.S. Patent No. 5, 914,393, to overcome this rejection and have requested an indication that such a filing is sufficient to overcome the rejection. As was previously stated, such a filing of a terminal disclaimer is sufficient to overcome this rejection. As was previously stated, such a filing of a terminal disclaimer would be sufficient to overcome this rejection, however, no TD has been filed at the present time, thus the rejection is maintained.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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July 29, 2002

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